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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,874	08/20/2003	Kenneth F. Buechler	071949-7002	8658

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EXAMINER	
LUM, LEON YUN BON	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 10/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,874	BUECHLER ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-33 and 43-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-33 and 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed August 16, 2006 is acknowledged and has been entered.

Information Disclosure Statement

2. The Yakovlev et al reference in the non-patent literature section of the IDS filed August 24, 2006 is not considered since this references has already been considered in a previous IDS.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 29, 32, 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Haffner et al (US 2004/0167341 A1).

Haffner et al teach a method for treating congestive heart failure by administering to a patient a compound that inhibits a dipeptidyl peptidase, including DPP-IV. See page 3, sections 0027-0028.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 30 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner et al (US 2004/0167341 A1) in view of De Meester et al (Biochemical Pharmacology, 1997).

The teachings of Haffner et al have been disclosed above, but fail to teach a phosphonate moiety.

De Meester et al teach Prodipine (Pro-Pro-diphenyl-phosphonate), in order to provide a compound that blocks DPP IV activity in both plasma and tissue with long-lasting results, and functions without affecting any other enzyme or producing any adverse effects upon the patient. See page 178, left column, 2nd-3rd full paragraphs.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Haffner et al by substituting the disclosed DPP-IV inhibitors with Prodipine, as taught by De Meester et al, in order to provide a compound that blocks DPP IV activity in both plasma and tissue with long-lasting results, and functions without affecting any other enzyme or producing any adverse effects upon the patient. The benefits of longer inhibition, wide range of applicability, and lack of adverse effects provide the motivation to combine the teachings of Haffner et al and De Meester et al. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in substituting the compounds of Haffner et al

with the Propidine of De Meester et al, since the compounds of Haffner et al are evaluated by their effect on DPP-IV plasma activity (see page 12, section 0174), and the Propidine of De Meester et al also functions to regulate DPP-IV levels in blood.

9. Claims 31 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner et al (US 2004/0167341 A1) in view of Bergmann et al (US 6,756,483 B1).

The teachings of Haffner et al have been disclosed above, but fail to teach a that the inhibitors of prolyl-specific DPP comprise an antibody or fragment thereof.

Bergmann et al teach that inhibitors to DPP-IV include suitable selective binders, antibodies, or similar receptor molecules. See column 3, lines 35-42.

The Courts have ruled that art-recognized equivalence between embodiments provides a strong case of obviousness in substituting one material for another. See MPEP 2144.06:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)

In regards to the instant application, the specification discloses the phrase "DPPs may also be inhibited through the use of binding proteins, **e.g.**, antibodies or fragments thereof that specifically bind to one or more DPPs and prevent their activity on a natriuretic peptide substrate." See page 16, section 0049. The specification therefore teaches that "antibodies or fragments thereof" are simply one example of binding embodiments that can inhibit DPP. There is no explicit disclosure indicating a preference for the "antibodies or fragments thereof" over other embodiments that perform the same function. While section 0074 covering pages 23-24 define the term "inhibitor", it does not mention the term "antibodies" nor disclose a benefit of antibodies over other types of inhibitors. Rather, the section teaches that the term "inhibitor" refers **generally** to "molecules that affect an enzymatic (*e.g.*, proteolytic) acitivity..." Furthermore, sections 0126-0130 spanning pages 40-41 clearly disclose that antibody or antibody fragments are simply one type of DPP inhibitor equivalent in function to other types of molecules. Sections 0126-0127 first disclose that "DPP inhibitors include the dipeptide analogues...", followed by section 0128 disclosing "DPP-inhibitory antibody or antibody fragments **may also find use** in the methods described herein." The specification therefore discloses that different types of DPP inhibitors can be applied to can be applied in lieu of one another and are not specific for any particular purpose or reason, but can be used interchangeably.

Because Bergmann et al reference teaches that selective binders, antibodies, and similar receptor molecules are recognized as equivalents applied for the same purpose, and Applicants have not provided evidence indicating why the different

molecule types cannot be considered art-recognized equivalents, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the antibodies, as taught by Bergmann et al, for the pyrrolidines of Haffner et al. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in substituting the antibodies of Bergmann et al in the method of Haffner et al, since the DPP inhibitors disclosed in Haffner et al are applied *in vivo,* and the antibodies of Bergann et al can also be applied *in vivo*.

10. Claims 33 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haffner et al (US 2004/0167341 A1) in view of Mills et al (Journal of the American College of Cardiology, 1999).

The teachings of Haffner et al have been disclosed above, but fail to teach that natriuretic peptides are also administered to the subject.

Mills et al teach the administration of Nesiritide (human b-type natriuretic peptide), in order to quickly maintain hemodynamic effects for patients with symptopmatice decompensated heart failure. See page 155, abstract and entire page of full text.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Haffner et al to include the administration of Nesiritide as taught by Mills et al, in order to quickly maintain hemodynamic effects for patients with symptopmatice decompensated heart failure. The benefit of being able to maintain stability in a patient provides the motivation to combine Haffner et al and Mills et al

reference. The combination also provides a two-pronged approach in administering the long-term treatment of Haffner et al with the immediate stabilizing treatment of Mills et al for patients suffering from symptomatic decompensated heart failure. Furthermore, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in combining the two methods since both methods complement and not inhibit each other. The Propidine of Haffner et al regulates DPP-IV activity and therefore would not have affinity for DPP-IV binding partners, including the Nesiritide of Mills et al.

Response to Arguments

11. Applicants' arguments, see pages 4-8 of the response (Remarks section), filed August 16, 2006, with respect to the rejection of claims 29-33 under 35 U.S.C. 112, 1st paragraph (written description) have been fully considered and are persuasive. The written description rejection of claims 29-33 has been withdrawn.

12. Regarding the comments on pages 8-9 of the Remarks, the previous objection to the IDS filed January 24, 2005 has been withdrawn. However, the International Search Reports listed in the IDS forms filed on November 22, 2004 and January 24, 2005, and the PTO-892 form listed in the IDS filed January 24, 2005 are still not considered since they are not proper non-patent literature that can be printed in a patent. Any references

listed in those forms should be cited and not the forms themselves; Applicants have already stated this understanding in the comments.

13. Applicant's arguments with respect to claims 29-33 and 43-46 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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